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Coronavirus disease 2019 in Latin American patients with multiple sclerosis

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Abstract

Patients with multiple sclerosis (MS) who present coronavirus disease 2019 (COVID-19) are of particular interest to neurologists. These patients have a neuroimmune disease and receive immunomodulatory or immunosuppressive therapies in the long-term. We present here data from 73 patients with MS and a confirmed diagnosis of COVID-19 from five Latin American countries. Fifteen patients (20.5%) were hospitalized and two patients died. The use of anti-CD20 therapies was the only risk factor associated to hospitalization and death. Despite the small sample size, this study highlights the awareness regarding therapeutic options for MS during the pandemic.

Key words

multiple sclerosis, pandemic, COVID-19, rituximab, ocrelizumab

Introduction

Coronavirus disease 2019 (COVID-19) is a pandemic condition recognized by the World Health Organization in March 2020 that continues to cause great concern around the world. Data on patients with multiple sclerosis (MS) who

present COVID-19 are being collected in specialized databases worldwide. One of these databases is MuSC-19, an Italian initiative resulting from the overwhelming number of COVID-19 cases that the country faced in the early stages of the pandemic [1]. MuSC-19 was opened to other countries and five Latin American countries included data from their 73 patients with MS and confirmed diagnoses of COVID-19. The objective of this correspondence is to present the observations from these patients.

Method

Data on individuals with MS and with suspected or confirmed COVID-19 in Latin America were retrospectively collected. We included adult MS patients who had been in contact with their neurologist because of confirmed or suspected infection with SARS-CoV-2 during the observation period (January 15, 2020 to April 10, 2021). The confirmed cases were those with a positive molecular test (RT-PCR on nasal and pharyngeal swabs) for SARS-CoV-2 or a positive serological test obtained at any point during the observation period; the suspected cases were those with radiological findings and/or symptoms highly suggestive of SARS-CoV-2 infection, according to medical judgment (cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia) and/or close contact with a confirmed COVID-19 case in the 14 days prior to the onset of symptoms. The study was approved by the Ethics Committee of Universidade Metropolitana de Santos, SP, Brazil. Other contributing institutions requiring individual approvals sought these through their own committees. Confidentiality of patients' personal information was guaranteed. Demographic and clinical characteristics at baseline were reported as counts and percentages, means with standard deviations or medians with ranges.

Univariate and subsequent multivariate logistic regression statistical analyses were performed to identify variables associated with hospitalization or death due to COVID-19. Independent variables with $p < 0.20$ in univariate analyses were included in the multivariate model. The strength of the associations was expressed as adjusted odds ratios (OR) with 95% confidence intervals (CI). The significance level was set at 0.05; and all statistical tests were two-tailed.

Results

The group of 73 patients originated from Brazil (32), Argentina (15), Chile (12), Mexico (8) and Ecuador (6). The patients' mean age was 40 ± 11.1 years; there were 23 males (31.5%); the patients were mostly white (78.1%); and the average body mass index (BMI) was 25.6 ± 5.08. Three patients smoked, nobody reported alcohol abuse and one patient reported occasional illicit drug use. There were ten cases of hypertension, two cases of cancer and one case of diabetes. The average MS duration was 7.5 ± 6.5 years, with a median EDSS of 2 (range, 0 to 8). Sixty-nine patients (94.5%) had relapsing-remitting MS and 70 patients (95.9%) were receiving MS therapy. Oral drugs (dimethyl fumarate, fingolimod, teriflunomide and cladribine) were used by 47.9% of the patients, auto-injectables (interferon beta and glatiramer acetate) by 27.4% and monoclonal antibodies (MAbs) (6 natalizumab, 1 alemtuzumab, 5 ocrelizumab and 3 rituximab) by 20.5%.

Only seven patients (9.6%) were asymptomatic during COVID-19. The most frequent symptoms of COVID-19 were fatigue (48.5%), fever > 38°C (47%), cough (42.4%), anosmia (24.2%), sore throat (22.7%) and headache (21.2%). All other symptoms affected less than 20% of the patients. Hospitalization was necessary for 15 patients (20.5%). In univariate analysis, use of anti-CD20

therapies seemed to be a risk factor for hospitalization compared with other treatments (OR = 7.00, 95% CI = 1.31-37.30, p = 0.023). In addition, male sex, progressive MS forms, presence of at least one comorbidity and recent use of methylprednisolone suggested an increased risk, although without reaching statistical significance.

In the multivariable model, presence of at least one comorbidity (OR = 4.70, 95% CI = 0.80-27.73, p = 0.09) and use of anti-CD20 therapies (OR = 5.74, 95% CI = 0.76-43.65, p = 0.09) remained the only factors indicating a risk of increased COVID-19 hospitalization and/or death; however, neither of these factors reached statistical significance.

When interferon beta and glatiramer acetate were used as reference drugs, there was a significant higher level of hospitalization and/or death among patients using anti-CD20 therapies (OR = 7.00, 95% CI = 1.31-37.30, p = 0.023). There were two cases of death: their characteristics are summarized in Table 1.

Table I – Characteristics of deceased patients

		Patient 1	**Patient 2**
Demography	*Country*	Ecuador	Mexico
	Sex, age	Female, 37 years	Male, 30 years
	Body Mass Index	23.7 kg/m^2	28.3 kg/m^2
	Ethnicity	Mestizo	Mestizo
	Pregnancy (present or past)	No	–
	Employment	Office clerk	Workman
	Number of cohabitants	None	2 (no children, no COVID)
	Smoking, alcohol consumption, substance abuse	No	No

	Comorbidities	No	Hypertension
MS history	*Type of MS, disease duration*	PPMS, 2 years	RRMS, 1 year
	Last EDSS	3.0	3.0
	MS treatment	Rituximab	Ocrelizumab
	DMD interrupted, and reason	No	Yes (due to COVID–19 infection)
	Previous treatment	No	No
	Recent use of methylprednisolone	No	No
	WBC and lymphocyte results	Normal	Normal
COVID, signs & symptoms	*Signs and symptoms*	Fatigue, chills, epigastric pain	Fever > 38, cough, fatigue, sputum production, sore throat
	Presence of pneumonia	Yes	Yes
	Potential exposure to source of transmission	Family	Work
	COVID laboratory tests	Confirmed Covid	Confirmed Covid
	Therapies during hospitalization	Intravenous antibiotics, systemic glucocorticoids, oxygen therapy	Intravenous antibiotics, systemic glucocorticoids, oxygen therapy
	Hospitalization	Yes	Yes
	ICU	Invasive ventilation	Invasive ventilation
	Cause of death	COVID-related complications	COVID-related complications

Discussion

Our study showed results like those from other cohort of patients with MS and COVID-19. However, the relative novelty of COVID-19 and the need for pharmacovigilance in MS therapies that affect patient immunity, encouraged us to report these data.

A recent Latin American study reported that there were no deaths associated with COVID-19 in a cohort of 129 patients with MS [2]. Older age and longer disease duration were the two factors associated with higher risk of hospitalization in this cohort. There was a similar experience in the Netherlands among 43 patients with MS who tested positive for COVID-19 [3]. A report on seven patients with MS and COVID-19 undergoing treatment with anti-CD20 even hypothesized a protective role for anti-CD20 MAbs during COVID-19 [4]. Internal Roche/Genetech data sources from clinical trials and real-world data identified 337 cases of confirmed COVID-19 in patients undergoing treatment with ocrelizumab [5]. Twenty-one patients (6.2%) died. However, the outcomes from 38.6% of patients with confirmed COVID-19 were missing from the final analyses of that paper.

In our study, patients with MS and COVID-19 progressed relatively well, except for two patients who died. One of them had elevated blood pressure and BMI, and both used anti-CD20 MAbs.

In the larger Italian cohort in MuSC-19 (n = 844 patients), older age, male sex, higher EDSS, longer MS duration, presence of at least one comorbidity, recent use of methylprednisolone, progressive MS course and use of anti-CD20 therapies were all associated with higher risk of greater severity of disease in univariate analysis [6]. Patients receiving anti-CD20 therapies have been shown to have higher risk of developing COVID-19 than patients receiving any other therapy for MS [7]. It must be noted that our data, despite the very small sample size, are very consistent with the Italian findings. A recent systematic review showed controversial data on higher mortality among patients with MS who had COVID-19 while on anti-CD20 therapies [8]. With the results from the present

Latin American cohort, we would like to emphasize the need for awareness regarding the use of anti-CD20 MAbs in patients with MS who are at risk of COVID-19. It remains to be seen how anti-CD20 MAbs will affect vaccine-related antibody responses in vaccination against COVID-19 [8].

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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